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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,873	07/31/2001	Elizabeth J. Goldsmith	A33864 090495.0232	2430
21003	7590	05/14/2004	EXAMINER	
BAKER & BOTTS 30 ROCKEFELLER PLAZA NEW YORK, NY 10112			NASHED, NASHAAT T	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/918,873

Applicant(s)

GOLDSMITH ET AL.

Examiner

Nashaat T. Nashed, Ph. D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 and 34-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32 and 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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The application has been amended as requested in the communication filed March 5, 2004. Accordingly, claim 32 has been amended.

This application contains claims 1-31 and 33-40 drawn to an invention nonelected with traverse in filed June 6, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 32 and 33 are under consideration as they relate to the embodiment of the protein kinase of p38.

Claim 33 is objected to under 37 CFR 1.75(d)(1) as being in improper form because the claim states an improper Markush group for the reasons set forth in the prior Office action mailed August 7, 2003.

Applicants argue that each member of the Markush group is a protein kinase that possesses the claimed inhibitor-binding site described in claim 32.

Applicants' arguments filed 3/5/04 have been fully considered but they are not deemed to be persuasive. The members of the Markush group are indeed protein kinases, which share no common structure or function. Each member of the Markush group has specific utility, which is catalyzing the transfer of a phosphate group from ATP to a specific protein substrate. Also, each member of the Markush group is an independent chemical entity having different amino acid sequence. While the inhibitor-binding site may be constructed from similar structural elements such as L5, helix C, L7 and betaL16, each one of these elements in each protein kinase has a distinct structure define by the amino acid residues within these structural elements. Thus, the members of the Markush group of claim 32 do not share a common function or structure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrase "protein kinase inhibitor binding site" in claims 32 and 33 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired for the reasons set forth in the prior Office action mailed August 7, 2003.

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Applicants argue that the Examiner allegedly finds two meanings to the claim, i.e., a polypeptide comprising residues 78-336 of SEQ ID NO: 1 and structure of the protein kinase inhibitor-binding site.

Applicants' arguments filed 3/5/04 have been fully considered but they are not deemed to be persuasive. The problem with the claim is that the examiner can't determine what is being claimed. Is it a polypeptide molecule or a domain of a protein? Is it a structural element? Is it the space between the various structural elements? The claims do not contain the phrase "a polypeptide comprising residues 78-336 of SEQ ID NO: 1". The amendment of the claim to be directed to "an isolated polypeptide fragment" would obviate this rejection.

- (b) Claim 32 attempts to define the protein kinase inhibitor-binding site by identifying three dimensional structure elements, but the specification contains no atomic coordinates for any protein kinase including p38 (the reference structure) which renders the claim indefinite for the reasons set forth in the prior Office action mailed August 7, 2003.

Applicants argue that the inhibitor binding site is defined by homologues regions in protein kinases and all is needed is to align the amino acid sequences of the protein kinases.

Applicants' arguments filed 3/5/4 have been fully considered but they are not deemed to be persuasive. Claim 32 states "has three-dimensional structural homology to protein kinase domain". Since the structure of the standard protein is undefined, one of ordinary skill in the art would determine be able to identify the structures which are homologues to the standard structure. Applicants should not the claim is directed to three-dimensional structural elements which would require three dimensional structures to identify their homology and not amino acid sequences.

- (c) Claim 33 contains references to several specific proteins, which are not identified by sequence identification numbers, which renders the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Applicants have not obviated this rejection or traverse it.

New Ground of Rejection:

- (d) The newly added phrase "an isolated protein kinase inhibitor-binding site" renders the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is not clear to the examiner from where the protein kinase inhibitor-binding site is isolated. Is isolated from a mammal? Is it a protein fragment? Is a model or computer representation of the inhibitor-binding site?

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35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 32 and 33 are rejected under 35 U.S.C. 101 because the claimed invention is directed toward non-statutory subject matter for the reasons set forth in the prior Office action mailed August 7, 2003.

In response to the above rejection, Applicants amended the claim to indicate that the binding site is "isolated" and argue that the amendment should obviate the rejection because the claim shows the hand of man. In addition, they argue the claim is not directed to a property of a protein as claim 32 relate to a molecule having specific structural features.

Applicants' arguments filed 3/5/4 have been fully considered but they are not deemed to be persuasive. As indicated above and in the previous Office action, the examiner can't determine with some certainty what is being claimed. If the claims are directed to a polypeptide molecule and composition thereof, they are directed to statutory subject matter. On the other hand, if the claims are directed to a structural elements, space between various atoms, or representation of collection of atoms, they are directed to non-statutory subject matter. The claims are not sufficiently clear for the examiner to determine what is being claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the prior Office action mailed August 7, 2003.

In response to the above rejection, applicants amended the claim and argue that applicants had possession of the claimed invention as they teach a method of obtaining the crystal of p38 with inhibitor, a method of determining the structure of protein kinase with inhibitors, determination of the crystal structure of inhibitor binding domain of p38, and essential inhibitor kinase domain of p38.

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Applicants' arguments filed 3/5/04 have been fully considered but they are not deemed to be persuasive. Although the examiner agrees with what the applicants have taught in the specification, the specification does not teach any three dimensional structure of any protein kinase or part thereof, a general method to obtain a crystal of any protein kinase comprising an inhibitor, and any inhibitor-binding domain other than that of p38. Applicants allege that the entire structure is not required to show possession of the claimed inhibitor-binding domain. Certainly, the entire structure may not be required, but, at least, part of it is. While Figures 4 and 5 are nice pictures in two dimensions, they are no substitute for atomic coordinates, which are required for constructing a three dimension dimensional model to identify the binding domain. Applicants are reminded with the text of claim 32, which states that "has three dimensional structural homology to". The claim contains a three-dimensional structure limitation, which is not disclosed in the specification. The various structure elements listed in claim 32 can be arranged in infinite number of ways, and thus, one of ordinary skill in the art would not be able to identify the true geometrical arrangements of the listed structural elements. Accordingly, one of ordinary skill in the art can't distinguish between the protein kinases containing the inhibitor-binding domain from those, which do not. Sequence alignment is not the same as three-dimension alignment, which the claim requires.

Claims 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure **is not even** enabling for the inhibitor-binding site of p38 for the reasons set forth in the prior Office action mailed August 7, 2003.

In response to the above rejection, applicants asserts that the claimed invention can be carried out without undue experimentation, and that the specification teaches a sufficient number of representative examples of the inhibitor-binding domain.

Applicants' arguments filed 3/5/04 have been fully considered but they are not deemed to be persuasive. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office action sets out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the disclosure to enable the scope of the instant claims. Applicants merely assert that no atomic coordinates are needed to practice the full scope of the claimed invention, and that all it takes, to practice the claimed invention is sequence alignment to identify the inhibitor binding site. As indicated above, sequence alignment is no substitute for three-dimensional structural alignment. As indicated above, the examiner can't determine what is being claimed, and therefore can't determine the full scope of the claimed invention. In writing the rejection, the examiner relied on guessing what is the full scope

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of the claimed invention. If the claim directed to a polypeptide/protein comprising an inhibitor-binding site, the specification contains some enabling embodiment. In contrast, if the claim is directed to a polypeptide consisting of p38 inhibitor-binding site, there is clearly lack of enablement because the specification does not teach any isolated peptide or polypeptide consisting of p38 inhibitor binding site. Other possibilities are the space wherein the inhibitor binds to the binding site and a three-dimensional model of the binding site neither of which is enabled in the specification. The examiner would like to be informed as to what entity the claims are directed. Are they directed to a chemical compound or composition, machine or a design?

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson *et al.* [J. Biol. Chem. 271, 27696-27700 (1996)] for the reasons set forth in the prior Office action mailed August 7, 2003.

Claims 32 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by U. S. Patent 6,387,641 [(641), Bellon *et al.*] for the reasons set forth in the prior Office action mailed August 7, 2003.

In response to the above rejections, applicants argue neither one of the references teach the inhibitor binding site.

Applicants' arguments filed 3/5/04 have been fully considered but they are not deemed to be persuasive. The examiner agrees with the applicants that neither one of the references teaches the inhibitor-binding site, but the inhibitor-binding site is an intrinsic property of the polypeptides or structures taught in the cited prior art. If the claimed invention is directed to a polypeptide comprising the inhibitor binding site domain, the claimed invention read on the polypeptide in both references. If applicants' claims are directed to a model comprising the inhibitor-binding site, the models taught in both references must contain the inhibitor-binding site. Applicants have not distinguished their invention from those taught in the prior art. Applicants should be reminded that discovering new characteristics of known compound would not make a known compound novel.

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No claim is allowed.

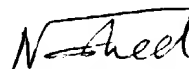
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.
Primary Examiner
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